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# RADIUM

EDITED BY
CHARLES H. VIOL, Ph. D.
AND
WILLIAM H. CAMERON, M. D.

VOL. XII FEBRUARY, 1919 No. 5

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Radioactivity Measurements. From the Annual Report of the Director of the Bureau of Standards.

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

# RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D. with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. XII FEBRUARY, 1919 No 5


## SQUAMOUS CELLED EPITHELIOMA RESPONDING TO ROENTGEN AND RADIUM THERAPY*


BUNDY ALLEN, M. D.

Roentgenologist, University Hospital, State University of Iowa, College of Medicine.


Patient 7694, C. S. W., dealer in insurance and real estate, white, American, single, 69 years old. First entered the Department of Eye, Ear, Nose and Throat, S. U. I. Hospital, in January, 1918.

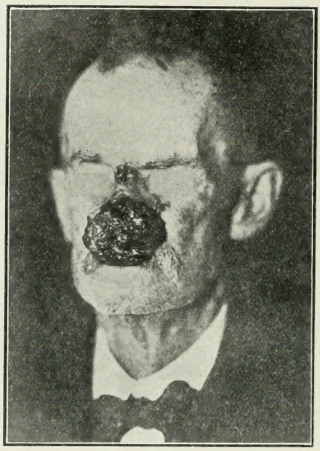
History: About eighteen months or two years ago a small pimple appeared upon the left side of the nose. This gradually grew larger, ulcerated, and at the end of six months was about the size of the thumb nail, discharging considerably. The growth continued to about the size of a small orange (Fig. One), at which time Roentgen and Radium therapy was advised.

About six years ago a similar growth developed on his right temple, and in two years had reached the size of a small egg. This was removed, and a skin graft operation performed at Johns Hopkins. For the past year there has been a small spot, about three-fourths of an inch in diameter, at the upper end of the graft. This has been rough and reddened.

Just over the bridge of the nose is a small rough elevated growth, about one inch by three-fourths of an inch; which started about a year ago as a small pimple and gradually grew. Patient has worn nose glasses about twenty years and this growth is just where the glasses rest.

About one and one-half inches below the left eye, and near the nose, is another small rough growth, which has been there four years, but has not grown any until recently. There has been very little pain with this trouble, and very little loss of weight. Two months ago he began to have difficulty in breathing through nose. There is no other

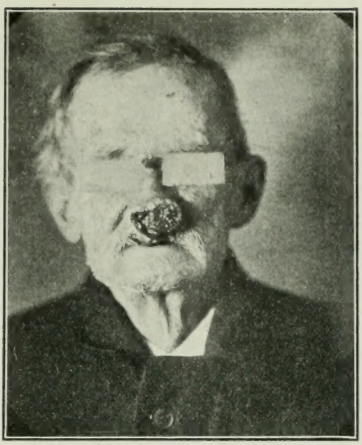

*Reprinted from the Journal of Roentgenology, I, 264-270- Oct., 1918.



Case 7694 W., Mr. C. W.
Squamous Cell Epithelioma

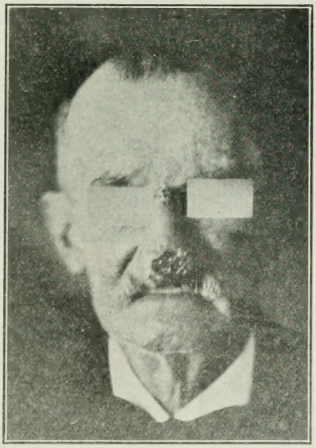
history of nose trouble. Eye, ear and throat history negative. Family history: Mother's sister died with carcinoma of the face. Father died of pulmonary tuberculosis at the age of fifty-six. Other family history, negative. Social history, negative. Examination: Nose appears enlarged in all dimensions and reddened. There is a shallow excavation on the end of the nose, just above the tip, and including the left lower

Case 7694 W., Mr. C. W.
December 15, 1917

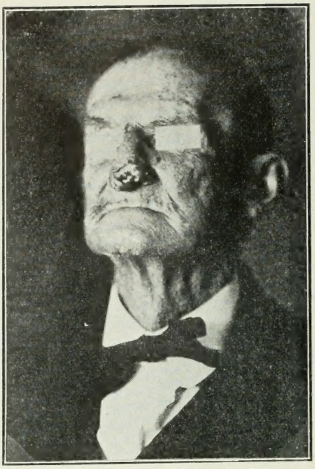


Case 7694 W., Mr. C. W.
January 12, 1918

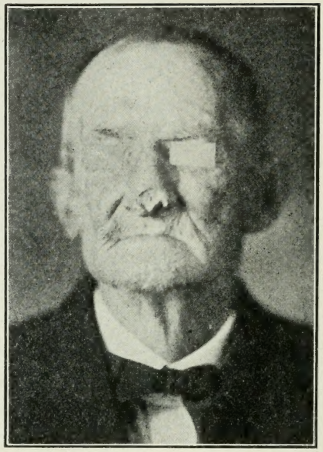
edge. The excavation is one inch by one-half inch and extends from one-fourth inch to the right of the mid line to three-fourths of an inch to the left of the mid line. Just above and to the left of the excavation is a dark spot, which is the location of the discharge of a few weeks ago. The left anterior nares is completely filled by a mass, the size of a large hazelnut. A similar growth is found in the upper part of the



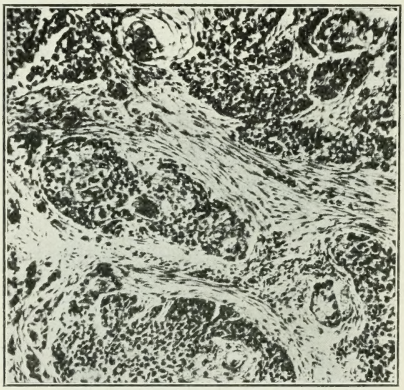
Case 7694 W., Mr. C. W.
February 2, 1918



Case 7694 W., Mr. C. W.
March 1, 1918

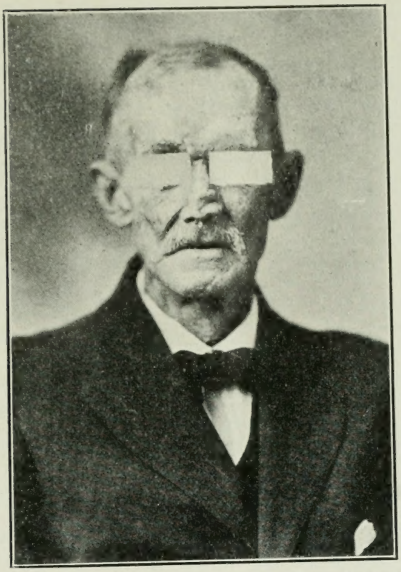


Case 7694 W., Mr. C. W.
March 14, 1918



Photomicrograph of Case 7694 Made with 1/6 Lens and No. 4 Eye Piece

right nares. On the bridge of the nose is a rough area, composed of several small nodules. The left face presents a reddened appearance. There is a skin graft on the right side of the face, with some reddened areas at upper and lower angles of the graft. There is a mucopurulent discharge from the left nostril. The growth in the nostril is rather firm and not attached except in its upper portion. On trans-illumination, antra and left frontal, clear. Right frontal cloudy. X-ray examination of the left accessory sinuses negative. Eye, ear and throat examination negative. Laboratory test negative.



This plate shows the result of the application of 1200 mililgram hours of radium and 1600 milliampere minutes roentgen therapy followed by rhinoplasty, as stated above.

Note made by Dr. Dean, that the external tumor mass has been removed by Roentgen and Radium therapy leaving white scar tissues. The tip of the nose is flattened, but the result is fine. Within the nose is a mass the size of a large hazelnut, rounded, hard and bleeds easily. Advise: Roentgen therapy and if no improvement, rhinoplasty. On June 19, 1918, rhinoplasty was performed by L. W. Dean, M. D., Iowa City, under ether anesthesia. Large pedical flap was taken from the forehead to form the nose. A tiersch graft from left thigh was used over exposed surface on forehead. The pathology report from section of nose showed squamous cell carcinoma. Hot dressings were used until August 3, 1918. At this time the flap on nose was well attached and there was no suppuration. There was some necrosis in the center of the tiersch graft, but this slowly granulated over and by the middle of September, 1918, the wounds were completely healed and the patient was discharged.

## REVIEWS AND ABSTRACTS

H. Z. Giffin, M. D. (Rochester, Minn.) Splenectomy Following Radium Treatment for Myelocytic Leukemia. Medical Record. XCIV, 1020-1023, December 14, 1918.

"The first case of splenectomy for myelocytic leukemia was reported

in 1866 by Bryant. His patient was in poor general condition and the spleen was very large; death occurred two and one-half hours after the operation. Bryant reported a second fatal case in 1867. The spleen in this instance was again very large and the general condition of the patient poor. Death occurred immediately after the operation."

"The history of splenectomy for myelocytic leukemia is a repetition of the history of Bryant's cases and is extremely tragic. From 1866 to 1900 the operation was not infrequently performed. Approximately 86 per cent of the patients on record died within a few hours of the operation. The patients for the most part were weak, toxic and anemic, with huge spleens and high leucocyte counts, and had insufficient vitality to respond favorably at a time when surgical treatment could be suggested and accepted. It is true that they were operated on when least could be expected. The experience of various surgeons was similar, and the conclusion naturally followed that splenectomy for myelocytic leukemia was in no sense a justifiable operation."

"Bessel-Hagen, in 1900, was able to collect forty-two cases of splenectomy for leukemia in which four patients temporarily recovered. Johnston, in 1908, collected seven cases that had been reported between the years 1900 and 1908, with the temporary recovery of two patients. The total number of splenectomies for leukemia to the year 1908 was, therefore, forty-nine, with the temporary recovery of only six patients. It is known that of the six patients who withstood the operation, four died later. One lived as long as eight months, another lived three and one-half years. From a practical standpoint, this experience meant a very prompt mortality of at least 96 per cent. Since the appearance of Johnston's paper, the surgical treatment of myelocytic leukemia has received almost no attention. McCowan (1915) reported two cases in which operation was done after preliminary treatment by means of arsenic and the x-ray. There was marked improvement in these patients three months after operation. The total number of cases reported in the literature to January 1, 1918, is, therefore, fifty-one, with eight temporary recoveries, an operative mortality of 86 per cent; four of the eight patients are known to have died later, giving a total known mortality of 93 per cent. Carstons has collected abstracts of all cases of splenectomy up to the year 1915. His article forms a complete and instructive resume of the subject; he presents protocols of many of the published cases of splenectomy for myelocytic leukemia."

"The remarkable remissions in the course of myelocytic leukemia, which can be produced by means of the exposure of radium element, or radium emanation, over the enlarged spleen, have been recently discussd by Ordway, Peabody, and the writer. The fact that the improvement following radium exposures occurred as a result of treatment over the spleen only, and not over the long bones or over any other structures, led to the inference that possibly a malfunction of the spleen might have more to do with the general condition of the patient than had been supposed. Moreover, if the spleen could be removed at a time when it was small and freely movable, and when the general condition of the patient was good, the operative mortality would doubtless be much less than it had been formerly. Again, the elimination of the spleen as a mechanical factor would remove one of the most troublesome features of the disease, and add to the patient's comfort. Naturally, in the light of the fatal former experiences, it was with considerable hesitation that splenectomy for myelocytic leukemia was resumed. The surgical treatment

of leukemia has been discussed recently by W. J. Mayo and D. C. Balfour."

"Cases—In August, 1909, at the Mayo Clinic the spleen was removed in the case of a man aged 45 (Case 27,414), whose leucocyte count was 11,000, and whose differential count showed no myelocytes. In August, 1911, two years later, the leucocytes were 64,500, with 14 per cent myelocytes. The patient died December 27, 1914, five years and four months after the operation, with the symptoms of cardiorenal insufficiency. The spleen in this case weighed 2500 grams. This was evidently a leukemia of a more chronic type, as splenomegaly had been present four years preceding the operation. The total length of the history was, therefore, at least nine and one-half years. In view of the condition of the patient at the time of the operation, it is possible that life was prolonged and the patient made more comfortable by splenectomy."

"September 2, 1916, a spleen weighing 1100 grams was removed from a woman aged 50 years (Case 171,009). There had been no previous treatment by means of radium or the x-ray. The leucocyte count was 203,000 with 4.7 per cent myelocytes. Thirteen days after splenectomy the count had become reduced to 47,400 with 15.7 per cent myelocytes. The leucocytes rose to 113,800 with 36 per cent myelocytes, 2 months after operation. The patient was in good general condition up to three hours prior to death, which occurred one year and three months after operation and was probably due to cerebral hemorrhage. The duration of the history in this case was approximately 3.5 years."

"Twenty patients with myelocytic leukemia have been splenectomized at the Mayo Clinic. The two patients just discussed did not have preliminary treatment by means of radium. The remaining eighteen patients, however, were treated by means of radium exposures over the spleen prior to splenectomy. The details of this method of treatment have been discussed in a former paper. The spleen in each case of this series of eighteen was very much reduced in size and the general condition of the patient was very much improved as the result of radium treatment. The eighteen patients have been operated on within the last eighteen months; the last one January 21, 1918."

"The operation itself has not proved difficult in cases of leukemia when the spleen was only moderately large; there have been few adhesions and but little embarrassment from hemorrhage. Postoperative complications have been absent save in one patient who died with peritonitis. Postoperative transfusion was necessary only once.

"The operative mortality for the entire group of twenty cases was one death, or 5 per cent. The operative mortality in the reported cases was 86 per cent. It is clearly demonstrated, therefore, that the operative mortality need not be high with proper preliminary preparation of the patient by medical means. A mortality of 5 per cent is lower than the average for splenectomy in general. Patients in remissions with only moderately large spleens are not serious operative risks, even though they had formerly had various forms of hemorrhage."

"Of the remaining nineteen patients who recovered from operation, nine have since died, from two months to one year and three months after operation (leaving out of account the early chronic case in which the patient lived five years and four months, with a total duration of history of nine years and six months). The total duration of history in eight of the nine fatal cases was from nine months to three years and six months. In seven of the eight it was more than two years."

"The length of life following splenectomy seems to vary most closely, with the total duration of the disease. Eight of the nine patients dying subsequent to operation presented a duration of the disease of over two years, while six of ten living patients presented a total duration of disease of less than two years. Two living patients had a chronic type of the disease, and presented a duration of symptoms of over ten years and over six years respectively. Aside from the chronic cases, then, when splenectomy has been performed there is no reason to infer that the disease runs more than its usual course of two or three years."

"Seven patients were operated on early in the disease, that is, less than six months from the time of definite onset; six of these are alive, five are in excellent, or very good condition. It is possible, though not likely, that in these early cases the results will be better than in the later ones; four or the six patients have already lived more than one year. Nothing, however, of a definite nature can be inferred from the fact that six of the seven are alive, inasmuch as the total duration of the disease in all of them is less than two years."

"It is worthy of note that in two cases of a chronic type the patients are alive ten months and one year and seven months respectively after splenectomy. The total duration of disease in these two patients has been six years and ten months and ten years and seven months respectively. The spleens were large and fibrous, and the leucocyte counts were not very high. Indeed, splenectomy may prove warranted in the very chronic types of the disease, from the standpoint of the patient's comfort, even though it be ineffectual in the prolongation of life."

"The ages ranged from twenty-four to fifty-six years and seemed to make no difference in mortality. In general, patients with the largest spleens at the time of operation have died first. This would probably indicate that these patients represented a more severe type of the disease. The average weight of the spleens of the patients who were first treated by radium, and who have died since splenectomy was performed, was 975.6 grams. On the other hand, those with the smallest spleens at the time of operation have, in general, lived the longest. The average weight of the spleens of these patients was 722.5 grams. Of twelve patients who lived one year or more after splenectomy, the average weight of the spleen at the time of operation was 800 grams; in nine patients who had had a very thorough course of radium treatment it was 498.3 grams."

"A period of improvement in the patient's general condition followed operation in all cases save three. This general improvement consisted of a feeling of well being, which may have been psychic, of an improvement in the appetite and the anemia, of a gain in weight, and a definite loss of the icteroid tint when it was present. The general condition in most instances was quite satisfactory before operation, so that one can not say definitely that splenectomy was the factor responsible for immediate improvement. Marked gain in weight was, however, almost a constant postoperative feature. The period of improvement was not of definite duration."

"The blood, after splenectomy, showed no definite alteration, with the exception of an increase in the relative percentages of both small and large "lymphocytes." This was apparently not secondary to the fluctuation of the leucocyte count itself. Its significance is undecided and the characteristics of these mononuclear cells require further study. It is to be learned whether they are of bone marrow origin or whether

splenectomy in reality stimulates the activity of lymphopoietic structures. In some instances there is a very marked decrease, temporarily in the number of myelocytes found after splenectomy."

"Two patients returned for observation after operation, and on examination were found to have enormously enlarged livers, which, however, gave no discomfort. The general condition and color were quite good in one of them."

TABLE I.—SPLENECTOMY FOR MYELOCYTIC LEUKEMIA.

| Case. | Age. | Sex. | Leucocytes Time of Operation. | Date of Operation. | Weight of Spleen. | Death Time After Operation. | Duration of Disease. |
|---|---|---|---|---|---|---|---|
| **OPERATIVE MORTALITY.** | | | | | | | |
| 216648 | 36 | F | 22000 | 1-21-18 | 1705 | 6 days | 1 yr. |
| **SUBSEQUENT MORTALITY.** | | | | | | | |
| 27414 | 45 | M | 11050 | 8-11-09 | 1514 | 5 yrs. 4 mos. | 9 yrs. 6 mos. |
| 171003 | 56 | F | 202000 | 9 -22-16 | 1100 | 1 yr. 3 mos. | 3 yrs. 6 mos |
| 173772 | 35 | M | 7800 | 12 -8-16 | 749 | 1 yr. | 2 yrs. 6 mos. |
| 175791 | 24 | F | 9600 | 1-18-17 | 750 | 1 mos. | 2 yrs. |
| 176684 | 26 | F | 13200 | 2-28-17 | 569 | 1 yr 2 mos. | 2 yrs. |
| 162899 | 32 | F | 37900 | 3 -8-17 | 1000 | 3 mos. | 9 mos. |
| 188262 | 50 | F | 22000 | 4-10-17 | 1340 | 8 mos. | 3 yrs. |
| 180199 | 42 | M | 5600 | 5-11-17 | 1300 | 2 mos. | 2 yrs. |
| 204838 | 53 | M | 11400 | 8-17-17 | 410 | 3 mos. | 2 yrs. 3 mos. |

May 1, 1918.

TABLE 2.—SPLENECTOMY FOR MYELOCYTIC LEUKEMIA: SUBSEQUENT CONDITION OF LIVING PATIENTS.

| Case. | Age. | Sex. | Leucocytes Time of Operation. | Date of Operation. | Weight of Spleen, Grams. | Condition. | Time After Operation. | Duration of Disease. |
|---|---|---|---|---|---|---|---|---|
| 168742 | 46 | M | 16400 | 9-19-16 | 2500 | Good | 1 yr. 7 mos. | 10 yrs. 7 mos. |
| 173312 | 33 | M | 3800 | 11-24-16 | 890 | Excellent | 1 yr. 6 mos. | 2 yrs. 6 mos. |
| 160937 | 37 | F | 68000 | 12-13-16 | 338 | Good | 1 yr. 5 mos. | 3 yrs. 5 mos. |
| 175574 | 37 | M | 15200 | 1-13-17 | 500 | Excellent | 1 yr. 3 mos. | 1 yr. 5 mos. |
| 169876 | 36 | F | 8400 | 1-27-17 | 220 | Fair | 1 yr. 3 mos. | 1 yr. 6 mos. |
| 177183 | 28 | F | 54400 | 2-17-17 | 410 | Good | 1 yr. 2 mos. | 1 yr. 8 mos. |
| 181494 | 19 | F | 7500 | 3-15-17 | 110 | Excellent | 1 yr. 1 mo. | 1 yr. 7 mos. |
| 186558 | 50 | F | 7200 | 4- 9-17 | 387 | Good | 1 yr. | 1 yr. 6 mos. |
| 193829 | 29 | M | 15400 | 6- 4-17 | 1420 | Good | 10 mos. | 6 yrs. 10 mos. |
| 199386 | 29 | F | 26000 | 7-26-17 | 220 | Excellent | 9 mos. | 11 mos. |

May 1, 1918.

"One patient (Case 180,499), who died two months after operation, and who had presented very slight enlargement of the glands, developed a remarkable glandular hypertrophy immediately after the operation, which persisted to the time of his death. The leucocyte count rose to 466,000, of which 63 per cent were small lymphocytes and 18.7 per cent were large lymphocytes, with only 3 per cent myelocytes. Before operation the small lymphocytes were as low as 3 per cent with 28.3 per cent myelocytes. The small lymphocytes rose steadily, however, after

radium treatment, to the time of operation, when they were 3 per cent with 0.3 per cent myelocytes. Two weeks after operation the small lymphocytes rose to 61.7 per cent, and the case if then seen for the first time would doubtless have been diagnosed as a lymphatic leukemia. Examination for oxidase granules in these cells was not made. A gland examined microscopically after death showed lymphocytic hyperplasia."

"*Summary*—1. Twenty patients with myelocytic leukemia have been splenectomized; eighteen of them after preliminary treatment by means of radium exposures over the spleen. The spleen and the leucocyte count were, by means of radium, very much reduced and the general condition of the patients was greatly improved."

"2. One patient died, an operative mortality of 5 per cent. The operative mortality of cases reported in the literature in which little or no preliminary medical treatment had been given was 86 per cent."

"3. Ten of the twenty patients are living in good general condition from nine months to one year and seven months following splenectomy. However, these patients have not yet outlived the life expectancy for the disease."

"4. Of seven patients operated on within six months of the time of the onset of the disease, six are alive."

"5. It is probable that, at least in certain chronic types of myelocytic leukemia with fibrous spleens and relatively low leucocyte counts, splenectomy may be justifiable for the comfort of the patient."

"6. A review of the cases at this time reveals no evidence that the duration of the disease is altered in any definite way by splenectomy. A detailed conception of the results following splenectomy may be obtained from an examination of Tables 1 and 2."

* * * * *

G. L. Rohdenburg and F. D. Bullock (New York). The Influence of Heat and Radium Upon Induced Immunity Against Transplanted Animal Tumors. The Journal of Cancer Research, III, 181-191, April, 1918. From Columbia University, George Crocker Special Research Fund, F. C. Wood, Director.

"In several publications, Bashford has called attention to the relationship existing between the growth energy of transplanted tumors and their power to induce the resistant state, and has also correlated the growth energy of these tumors with their resistance to the immunizing action of living cells. Broadly stated, his viewpoint is: That the power to overcome the resistant state varies directly as the growth energy of the tumor, whether immunity result from the growth of the tumor itself (concomitant immunity) or be caused by normal living cells."

"If Bashford's view be the correct one, then it should be possible to immunize against tumors which are refractory to the induced resistant state, and to increase the percentage of induced immunity against susceptible tumors, by depressing the growth energy of these neoplasms. This has, in fact, been done by Tsurumi, who has demonstrated that certain sarcomata which are resistant to induced immunity can be rendered susceptible by exposing them to comparatively low degrees of heat for varying periods before inoculation. It should also be possible to bring out more distinctly the concomitant immunity produced by various growing tumors."

"The growth energy of transplanted tumors can be depressed, also, by radium, as Wedd and Russ and Wood and Prime have shown. The retardation of growth energy was not a permanent alteration in the biology of the tumor, however, and persisted only for a few generations of transplants."

"With these facts in mind, a series of observations upon the influence of radium and heat in induced immunity was undertaken with various tumor strains. The strains chosen were the Crocker Fund mouse sarcoma 180 and the Ehrlich mouse sarcoma, both refractory to the immunizing power of living cells, and the Jensen rat sarcoma, which is susceptible to the induced resistant state."

"The technic used in depressing the growth energy of the tumors was as follows: 83 mgm. of radium element, screened by 0.4 mm. of brass and a thin glass cover-slip, were placed upon a strip of tumor 2 mm. trick, 2 to 3 mm. wide, and 20 mm. long, so that the screened radium capsule was superimposed upon the tumor material, strict aseptic precautions being observed. The exposure to radium was continued for thirty minutes."

"When heat was used, strips of tumor of dimensions similar to those of the strips exposed to radium were placed in Ringer's solution in the incubator at 38°C. for two hours."

"Portions of the tumor strain to be used in a given series were treated by radium or heat to depress their growth energy, according to the technic just described. Inoculations by needle of 0.003 gram of the treated tumor were made into one group of animals immunized ten days previously with 0.05 cc. of spleen emulsion, and into another series of animals not immunized. These two series gave the percentage of induced and natural immunity with treated tumor. Another group of animals immunized ten days previously with spleen emulsion, in doses of 0.05 cc., were inoculated with 0.003 gram of the untreated tumor by needle. A final group of nonimmunized control animals was inoculated with similar doses of the untreated tumor at the same time. The last two groups inoculated with untreated tumor served to show the percentages of natural and induced immunity for the untreated neoplasm."

"In order to control the influence of the immunizing agent, the experiment was repeated with a fourth tumor strain, the English mouse carcinoma 199, a neoplasm which is moderately resistant to the immunizing power of living cells (Russell, (5). The technic and method used with this strain differed from that previously described only in that fetal skin emulsion was used instead of splenic pulp."

"Table 1, which gives the numerical data of each experiment, shows that depression of the growth energy of the four tumor strains chosen, whether caused by radium or heat, results in a marked increase in their susceptibility to the immunity produced by splenic pulp. The percentage of induced immunity against untreated tumor, as averaged for all four strains, was 29.25, while the groups immunized and inoculated with radiumized tumor showed an average of 62.75 per cent and those immunized and inoculated with heated tumor showed 81 per cent average immunity, an increase of over 100 per cent in both treated groups. As is shown in both the table and the charts, our results were not influenced by the type of immunizing material used. It will also be noted in the charts that the growth energy of the treated tumors was depressed, their size on a given day being smaller than the untreated neoplasms."

"The fact having been verified that depression of growth energy renders tumors more susceptible to the immunizing power of homologous

living normal cells, it was determined to investigate the influence of depression of growth energy upon other phases of immunity."

"In the succeeding experiments radium was used to depress the growth energy."

TABLE I.

| | | TUMOR STRAIN | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 180 | | 199 | | Ehrlich sarcoma | | Jensen sarcoma | |
| | | -\|- | — | -\|- | — | -\|- | — | -\|- | — |
| Normal controls inoculated with normal tumor | Number | 88 | 1 | 20 | 7 | 16 | 10 | 18 | 1 |
| | Per cent | 99 | 1 | 74 | 26 | 61 | 39 | 95 | 5 |
| Immunized controls inoculated with normal tumor | Number | 60 | 16 | 13 | 9 | 9 | 1 | 14 | 11 |
| | Per cent | 78 | 22 | 59 | 41 | 90 | 10 | 56 | 44 |
| Normal animals inoculated with radiumized tumor | Number | 90 | 2 | 16 | 3 | 20 | 1 | 18 | 6 |
| | Per cent | 98 | 2 | 84 | 16 | 94 | 6 | 75 | 25 |
| Immunized animals inoculated with radiumized tumor | Number | 37 | 35 | 8 | 38 | 3 | 3 | 2 | 18 |
| | Per cent | 51 | 49 | 18 | 82 | 50 | 50 | 10 | 90 |
| Normal animals inoculated with heated tumor | Number | 17 | 2 | 17 | 6 | 21 | 1 | 13 | 10 |
| | Per cent | 89 | 11 | 73 | 27 | 95 | 5 | 57 | 43 |
| Immunized animals inoculated with heated tumor. | Number | 4 | 8 | 0 | 14 | 3 | 7 | 8 | 16 |
| | Per cent | 12 | 88 | 0 | 100 | 30 | 70 | 34 | 66 |

-|- = takes.
— = no take.
Number = actual number of animals used.
Per cent = percentage of takes or immunity as the case may be.

"That the resistance of a graft to concomitant immunity is decreased by radium is shown in the following experiment. Thirty-three rats bearing eighteen day old Flexner-Jobling carcinomata were divided into two groups. This tumor under ordinary conditions does not produce concomitant immunity. One group of eighteen animals received a second inoculation of 0.003 gram of the same tumor strain, the inoculated material having been exposed to radium in the manner described in a previous paragraph. The second group of fifteen animals was inoculated with a similar dose of the same tumor not exposed to radium. A control group of ten normal animals was also inoculated with radiumized tumor."

"The results show 44 per cent concomitant immunity in the group inoculated with radiumized tumor, as compared with 20 per cent concomitant immunity in the group inoculated with normal tumor. The normal animals inoculated with radiumized tumor also exhibited 20 per cent natural immunity, showing that radiation had not killed the tumor."

"The influence of radium upon the processes of induced immunity was studied in still another experiment. A series of rats was inoculated with the usual dose of the Flexner-Jobling tumor. Five days after inoculation, the stroma reaction being established, the skin over each graft was exposed for five minutes to 83 mgm. of radium element, unscreened. Upon the same day one-half of this group (36 rats) was injected with 0.05 cc. of rat spleen emulsion, the other half of the group serving as controls. The animals were immunized on the day of radiation so that

both radium and immunity might exert their maximum effect simultaneously, i. e., about the tenth day."

"A further control group of 30 animals which had been inoculated at the same time as the other two groups was also immunized with 0.05 cc. of rat spleen pulp."

"As is shown in chart 6, twenty-six days after radiation the tumors had disappeared in 25 per cent of those radiated and immunized, as compared with 27 per cent in those radiated but not immunized. As the chart shows, the two groups with radiated tumors shows inhibition of tumor growth as compared with the nonradiated animals, though radiation had not been sufficient to kill the tumor completely. A tumor having once been established, therefore, the retardation of its growth energy by radium does not make it any more susceptible to immunity than are growing tumors that have not been radiumized, a result in complete accord with the previous work of Russell, who used untreated tumor. As the established tumor which has been radiumized is not subject to immunity reactions, it is much less probable that the tumor which has not been radiumized is in any way sensitive to immunity reactions. This observation, therefore, casts doubt upon the power of radium or x-ray to affect metastases of tumors at a distance from the growth radiated, as has been repeatedly claimed by clinical workers. Clinicians have stated that the radiumization of a primary breast tumor causes nodules in the axilla to disappear, and have proposed the hypothesis that ferments are set free from the primary tumor under the influence of the radiumization which act in an unfavorable manner upon masses at a distance from the primary growth. The experiments detailed above, however, show that the shrinkage and disappearance of such nodules—if they really do disappear—must be due to some other influence than the hypothetical ferment. The very great susceptibility of lymphoid tissue to even slight radiation is well known, and any change in the size of the lymph-nodes, even if they are invaded by carcinoma, may be due to reduction of inflammatory edema and to the destruction of the lymphoid elements, thus leaving the carcinoma untouched. This latter phenomenon has been repeatedly observed where clinical cures have been obtained of carcinomatous nodules, a marked shrinkage taking place upon relatively slight radiation. If such nodes are excised and examined, it is found that the lymphoid tissue has disappeared, but that the carcinoma, which forms only a small portion of the total mass, has remained as active in its growth as ever; and, in fact, those cases which have been followed have shown that ultimately recurrence takes place, even though the nodule after radiation was greatly reduced in size."

"In a final experiment, the possibility of making tumors susceptible to attempts to immunize with heterologous and autologous tissue was investigated. Although some investigators have described the appearance of immunity after the introduction of heterologous tissues, the majority have not succeeded in confirming their results; and almost all are agreed that autologous tissues are powerless to confer immunity."

"The Flexner-Jobling rat carcinoma was the tumor chosen for this experiment, the radiation, the inoculation dosage, and the methods being the same as those described in the early paragraphs of this paper. The

animals were divided into several groups, the rats of the first series being immunized with 0.05 cc. of skin taken from the animals themselves, those of the second series with 0.05 cc. of mouse carcinoma, while those of the third series were not immunized. Ten days after immunization, one-half of the animals of each series were inoculated with untreated tumor, the other half receiving inoculations of radiumized tumor. Thirty-one days after inoculation, our results showed that exposure to radium did not make the Flexner-Jobling carcinoma susceptible to either autologous or heterologous tissues. The numerical data of the experiments are given in table 2."

TABLE II.

| | No. of Animals | Percentage of Immunity |
|---|---|---|
| Normal animals with normal tumor | 19 | 0 |
| Normal animals inoculated with radiumized tumor | 20 | 5 |
| Immunized with mouse carcinoma, inoculated with normal tumor | 20 | 10 |
| Immunized with mouse carcinoma, inoculated with radiumized tumor | 33 | 9 |
| Immunized with autologous skin, inoculated with normal tumor | 15 | 10 |
| Immunized with autologous skin, inoculated with radiumized tumor | 12 | 4 |

*"Conclusions.* Depression of the growth energy of a transplantable tumor by heat or by exposure to radium increases its susceptibility to the immunizing action of homologous living cells, whether they be normal or tumor cells. With the technic as described in this paper the additional immunity thus obtained may be 100 per cent over the usual figure."

"The increased susceptibility of treated tumor to the immunizing power of living cells is not in evidence when autologous elements are employed, or when homologous tissues are introduced subsequent to tumor implantation."

"Tumors which have established a residence in their hosts, i. e., have excited a stroma reaction and obtained a blood supply, are not influenced by retardation of their growth energy with radium and the simultaneous introduction of homologous living cells."

"Thus, none of these results leads in any way to the conclusion that the improvement described in human cancer under radium treatment is due to the stimulation of autologous cells or that benefit is to be expected by radiumization and previous or subsequent injection of homologous lymphoid tissue. Even though the tumors employed in these experiments had been cured, the results could not have been transferred to man, where the problem is to cure a spontaneous (as distinguished from a transplanted) neoplasm. As an animal can not be immunized against its own tumor, or with its own tissues, it is readily seen that the application of such experiments as these to man can hardly lead to a profitable result."

* * * * *

Radioactivity Measurements. From the Annual Report of the Director of the Bureau of Standards, for the Year Ending June 30th, 1918. Pages 49-51.

*"Luminous Materials.* Both the apparatus for and the technique

of the measurement of the brightness of self-luminous materials have been much improved during the year. The fifty preparations under study in June, 1917, and a few others obtained since then have been measured at intervals. The conclusions drawn from these measurements have been made available to the military authorities interested in such materials."

"These materials are largely used for airplane instrument dials. Since little information regarding the brightness needed for satisfactory legibility of dials was available, the Bureau arranged to have a number of dials of various known brightnesses examined under service conditions of illumination by members of the air service of the United States and allied nations. A better idea of the brightness desired under different conditions was thus obtained. The variation of the legibility with the size and brightness of the characters has also been studied."

"The conclusions thus reached have been used, and passed on to those interested, as rapidly as obtained and are now being collated in a series of recommended specifications for luminous articles."

"Regarding the permanence of luminous material under service conditions little was known. It was believed that in general, an exposure to direct sunlight markedly decreased the brilliance of applied material. Observations made during the past winter have, however, shown no very marked decrease in brightness, due to an exposure either to the sun or to a mercury arc. The dials used in this test were of low brightness. Similar tests upon other dials will be begun at once."

"Specifications for luminous markings upon airplane dials have been recommended to the Signal Corps, United States Army, the Bureau of Steam Engineering, United States Navy, and informally to other departments of the Government. These specifications have been in the main adopted by the Signal Corps."

"Since September, 1917, the brightness of a large number of dials has been measured for the Science and Research Division of the Signal Corps, United States Army, (recently transferred to the Bureau of Aircraft Production), as a basis for the awarding of contracts for the illumination of airplane instruments."

"At the request of the Inspection Department of the Signal Corps, the Bureau has prepared and standardized equipment for factory inspection of dials, and has instructed inspectors in the details of factory testing. Since this equipment has been in use, brighter dials have been secured."

"Since the first of January, 1918, a percentage of the luminous dials accepted by the Inspection Department has regularly been sent to the Bureau for careful measurement of brightness. Certain of the dials have been submitted to a life test, and a number of compass cards have been measured both dry and submerged in kerosene. The effect of continued immersion in kerosene also has been studied. The cause of some of the changes observed on immersion is still not clear; the study is being continued."

"An investigation of methods for applying luminous materials to dials and other objects was undertaken late in November. Luminous materials were obtained from the different manufacturers and were applied to dials by means of various adhesives and methods. The various characteristics of the different adhesives and methods were noted and the brightness of the finished product was measured. The problem was

studied from many angles and a method of application that is more efficient than any now in use was developed."

"The following reports have been issued: "Self-Luminous Materials Containing Radioactive Excitants," "Notes and Suggestions Concerning Luminous Instruments," "Self-Luminous Materials—Brief Notes Covering a Few Points of Practical Importance." All of these were typewritten reports issued in editions of a few copies each and have been distributed to those Government departments that have appeared to be most interested."

"Throughout this work the co-operation of the manufacturers and users of these materials has been most gratifying and of great assistance to the bureau."

*"Standard Radium Solutions.* Incidental observations indicate that the standard radium solutions made up in the summer of 1914 have not changed by as much as 1 per cent since they were prepared."

"During the year, 100 cubic centimeters of the dilute solution ($10^{-8}$ gram of radium per cubic centimeter of solution) were furnished to McMaster University, Canada."

*"Radium Emanation Work.* The work involving radium emanation measurements is mainly the examination of materials suspected of radioactivity, of waters (natural and artificial), and of therapeutic preparations. No steps have been taken to encourage the development of this branch of the work, because all the facilities available could be used to advantage in more urgent lines."

"During the year 1 activator has been tested, the study of 4 others has been completed, and 5 radium determinations have been made; 2 of the latter were for the Department of Agriculture."

*"Gamma-Ray Measurements of Radium.* In July, 1917, the Bureau of Mines donated to the Bureau the tube containing about 49 milligrams of radium which was loaned to the Bureau of December, 1916, and also a second tube containing about 91 milligrams. Further than this, no change has been made in the equipment for this work."

"Early in 1918 the rate of receipt of specimens for gamma-ray measurement decreased markedly and has remained low. The amount of material for certification to physicians is now very small on account of war conditions."

"During the year 177 specimens, containing a total of 5,376 milligrams, have been measured. Of these, 50 specimens containing a total of 1,009 milligrams were certified for foreign department. These were distributed as follows:

| Country | Number | Milligram radium |
|---|---|---|
| France | 24 | 651.55 |
| Japan | 11 | 207.19 |
| Spain | 12 | 129.55 |
| India | 3 | 20.38 |

"Most of the radium certified for export to France is said to be for the use of the French Government in the manufacture of self-luminous material for war purposes. Two tubes (74.1 miligrams) were certified to the American Red Cross Society; it was understood that these were intended for the Russian Government."

* * * * *

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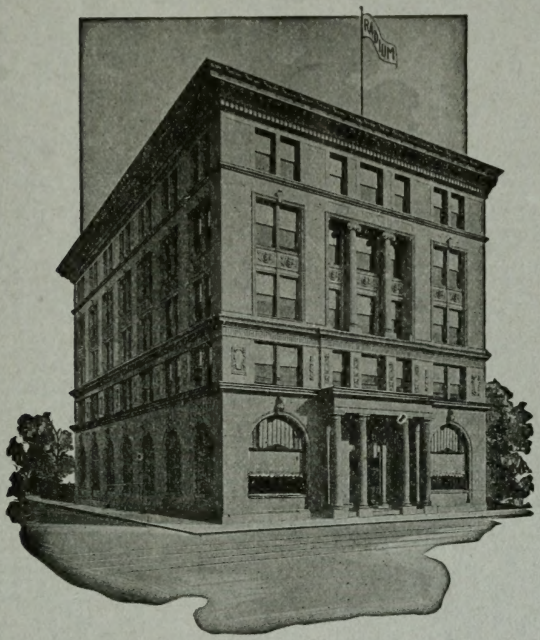


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